

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**204640Orig1s000**

**PROPRIETARY NAME REVIEW(S)**

**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Surveillance and Epidemiology  
Office of Medication Error Prevention and Risk Management**

**Proprietary Name Review**

Date: December 6, 2013

Reviewer: Teresa McMillan, PharmD  
Division of Medication Error Prevention & Analysis

Team Leader: Lubna Merchant, PharmD, M.S.  
Division of Medication Error Prevention & Analysis

Drug Name(s) and Strength(s): Adrenalin (Epinephrine Injection, USP)  
1 mg/mL

Application Type/Number: NDA 204640

Applicant/sponsor: JHP Pharmaceuticals

OSE RCM #: 2013-2445

\*\*\* This document contains proprietary and confidential information that should not be released to the public.\*\*\*

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## 1 INTRODUCTION

This review evaluates the proposed proprietary name, Adrenalin, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

## 2 PRODUCT INFORMATION

Adrenalin is currently marketed as a single-dose intramuscular, subcutaneous, and intraocular injection in a 1 mL vial at a concentration of 1 mg/mL. The proposed 30 mg/30 mL [1 mg/mL] multi-dose vial is to be administered via the intramuscular and subcutaneous routes only. Table 1 below provides a comparison of the proposed product to the marketed product.<sup>1</sup>

Table 1. Comparison of the Proposed Product With the Marketed Product		
Product Name	<i>Adrenalin (proposed)</i>	<i>Adrenalin (marketed)</i>
Approval Year	---	2012
Active Ingredient	Epinephrine	Epinephrine
Indication of Use	Hypersensitivity Reactions: Emergency treatment of allergic reactions, including anaphylaxis	<ul style="list-style-type: none"> <li>Hypersensitivity Reactions: Emergency treatment of allergic reactions, including anaphylaxis</li> <li>Ophthalmic Use: Induction and maintenance of mydriasis during intraocular surgery</li> </ul>
Route of Administration	Intramuscular and Subcutaneous	Intramuscular, Subcutaneous, and Intraocular
Dosage Form and Packaging	Injection [Multi-dose vial]	Injection [Single-dose vial]
Strength and Concentration	30 mg/30 mL [1 mg/mL]	1 mg/mL
Dose and Frequency	<p><b><u>Anaphylaxis</u></b></p> <p>Adults and Children [30 kg (66 lbs)] or more:</p> <ul style="list-style-type: none"> <li>0.3 mg to 0.5 mg (0.3 mL to 0.5 mL) intramuscularly (or subcutaneously) into anterolateral thigh every 5 to 10 minutes as necessary.</li> </ul> <p>Children less than [30 kg (66 lbs)] or less:</p> <ul style="list-style-type: none"> <li>0.01 mg/kg (0.01 mL/kg), up to 0.3 mg (0.3 mL), intramuscularly (or subcutaneously) into anterolateral thigh every 5 to 10 minutes as necessary.</li> </ul>	<p><b><u>Anaphylaxis</u></b></p> <p>Adults and Children [30 kg (66 lbs)] or more:</p> <ul style="list-style-type: none"> <li>0.3 mg to 0.5 mg (0.3 mL to 0.5 mL) intramuscularly (or subcutaneously) into anterolateral thigh every 5 to 10 minutes as necessary.</li> </ul> <p>Children less than [30 kg (66 lbs)] or less:</p> <ul style="list-style-type: none"> <li>0.01 mg/kg (0.01 mL/kg), up to 0.3 mg (0.3 mL), intramuscularly (or subcutaneously) into anterolateral thigh every 5 to 10 minutes as necessary.</li> </ul> <p><b><u>Intraocular Surgery</u></b></p> <ul style="list-style-type: none"> <li>Dilute 1 mL with 100 mL to</li> </ul>

<sup>1</sup> Information obtained from NDA 204640 October 23, 2013 submission.

		1000 mL of an ophthalmic irrigation fluid, for ophthalmic irrigation or intracameral injection. After dilution in an ophthalmic irrigating fluid, Adrenalin may also be injected intracamerally as a bolus dose of 0.1 mL at a dilution of 1:100,000 to 1:400,000 (10 mcg/mL to 2.5 mcg/mL). <b>NOTE: Adrenalin 1 mg/mL, 30 mL multi-dose vial is not for ophthalmic use.</b>
<b>How Supplied</b>	Carton of 1 or 10 multi-dose vials -30 mL solution in a 30 mL amber vial of Adrenalin	Carton of 25 single-use vials-1 mL solution in a 3 mL clear vial of Adrenalin
<b>Container and Closure System</b>	USP Type I glass vials with a rubber stopper and 20 mm Blue flip-off cap (for the 30 mL vial)	USP Type I glass vials with a rubber stopper and a 13 mm Purple flip-off cap (for the 1 mL vial)

### 3 FAERS DATABASE SEARCH

A FAERS search was not conducted for this review because we completed a Label, Labeling, and Packaging Review (#2013-2054 dated November 19, 2013) for Adrenalin. In that review, we did not identify any name confusion associated with the proprietary name Adrenalin.

### 4 PROPRIETARY NAME ASSESSMENT

#### 4.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Pulmonary, Allergy and Rheumatology Products (DPARP) concurred with the findings of OPDP's promotional assessment of the proposed name.

#### 4.2 SAFETY ASSESSMENT

This product contains the same active ingredient as the marketed Adrenalin. However, the proposed 30 mL multi-dose presentation and the marketed 1 mL single-use presentation differ in both qualitative and quantitative aspects [i.e., concentrations of inactive ingredients, preservatives, volume] and overlap in routes of administration and indications of use. Although these are important differences between the proposed product and the marketed Adrenalin, we agree with the applicant's proposal to use the same proprietary name for the following reasons:

- There is no difference in the concentration of the active ingredient or manufacturer. However, this product contains slightly different concentrations of inactive ingredients, a preservative (Chlorobutanol), and a larger volume (30 mL).

Due to the volume and the preservative, this product is inappropriate for the ophthalmic indication of use and intraocular route of administration for epinephrine. According to the clinical reviewer, these differences are minor and not an issue and both products are considered the same. In addition, this product will be added to the marketed Adrenalin insert. This combined insert will delineate the product differences and there will be statements added to the container labels and carton labeling highlighting the difference in routes of administration and volume.

- Other options for naming this product such as utilizing a different proprietary name or adding a modifier to the name Adrenalin are also error prone. Pursuing a different name for the same product from the same manufacturer could lead to concomitant therapy between this product and the currently marketed Adrenalin if healthcare practitioners and patients fail to recognize that both products contain Epinephrine. With respect to the addition of a modifier, it would be difficult to find an appropriate modifier that would convey the product differences (e.g. concentration of inactive ingredients, preservatives, routes of administration and volume, etc.) and distinguish it from the marketed Adrenalin.
- Although this nomenclature approach is not free from the risk of error, it offers a safer approach to naming this product.

#### ***4.2.1 Communication of DMEPA's Analysis at Midpoint of Review***

DMEPA communicated our findings to the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) via e-mail on December 6, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the (DPARP) on December 6, 2013, they stated no additional concerns with the proposed proprietary name, Adrenalin.

## **5 CONCLUSIONS**

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Nichelle Rashid, OSE project manager, at 301-796-3904.

### **5.1 COMMENTS TO THE APPLICANT**

We have completed our review of the proposed proprietary name, Adrenalin, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your October 23, 2013 submission is altered, the name must be resubmitted for review.

## **APPENDICES**

### **Appendix A**

#### **DATABASE DESCRIPTION**

##### **FDA Adverse Event Reporting System (FAERS)**

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's post-marketing safety surveillance program for drug and therapeutic biologic products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. The suspect products are coded to valid trade names or active ingredients in the FAERS Product Dictionary (FPD).

FDA implemented FAERS on September 10, 2012, and migrated all the data from the previous reporting system (AERS) to FAERS. Differences may exist when comparing case counts in AERS and FAERS. FDA validated and recoded product information as the AERS reports were migrated to FAERS. In addition, FDA implemented new search functionality based on the date FDA initially received the case to more accurately portray the follow up cases that have multiple receive dates.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether or not an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.

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/s/  
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TERESA S MCMILLAN  
12/06/2013

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12/09/2013